

AMENDMENTS TO THE CLAIMS

The following claim listing will serve to replace all prior versions of the claims in the subject application.

1. (Currently amended) A genetically modified non-human organism, wherein the genetic modification comprises the insertion of a reporter molecule-encoding sequence into an allele of the endogenous *Blimp* (*PRDM-1*) gene thereby creating a modified *Blimp* allele, and ~~wherein~~ expression of a polypeptide comprising the reporter molecule from the modified *Blimp* allele is under the control of endogenous *Blimp* regulatory elements, and wherein said genetically modified non-human organism is capable of producing functional Blimp protein.

2. (Previously presented) The organism of claim 1, wherein the modified *Blimp* allele encodes an mRNA transcript comprising a Blimp coding sequence and a reporter molecule coding sequence.

3. (Previously presented) The organism of claim 1, wherein the reporter molecule coding sequence is inserted within an intron of a *Blimp* allele.

4. (Previously presented) The organism of claim 1, wherein the modified *Blimp* allele is present in homozygous form.

5. (Previously presented) The organism of claim 1, wherein the modified *Blimp* allele is present in heterozygous form.

6-7. (Canceled)

8. (Previously presented) The organism of claim 1, comprising genetic material derived from an organism selected from the group consisting of man, non-human primates, livestock, companion or laboratory test organisms, reptilian, and amphibian species.

9. (Previously presented) The organism of claim 8, derived from a laboratory test animal selected from the group consisting of a rodent, guinea pig, pig, duck, rabbit and sheep.

10-12. (Canceled)

13. (Previously presented) The cell of claim 50, wherein the cell is a cell of the lymphocyte lineage selected from a B-cell and a T-cell.

14. (Previously presented) The cell of claim 13, wherein the B-cells are antibody secreting cells (ASC).

15. (Original) The cell of claim 14, which is a substantially purified population of ASC.

16. (Currently amended) The cell of claim 13, wherein the T-cells are selected from CD4⁺ T-cells ~~or and~~ CD8⁺ T-cells.

17-18. (Canceled)

19. (Previously presented) The cell of claim 50, wherein the reporter molecule is a fluorescent or light emitting reporter molecule.

20. (Currently amended) A method for ~~identifying~~isolating antibody secreting cells from a population of genetically modified cells, comprising:

- i) providing a population of genetically modified haematopoietic cell or non-human animal comprising said cellcells, wherein the genetic modification comprises the insertion of a reporter molecule-encoding sequence into an allele of the endogenous *Blimp* (*PRDM-1*) gene thereby creating a modified *Blimp* allele, and wherein expression of a polypeptide comprising the reporter molecule from the modified *Blimp* allele is under the control of endogenous *Blimp* regulatory elements[.,,];
- ii) detecting activity of the reporter molecule activity from saidin the population of

genetically modified cells ~~cell or non-human animal~~, and;

iii) ~~identifying-isolating~~ antibody secreting cells within the population of genetically modified cells based on activity of the reporter molecule activity.

21. (Canceled)

22. (Currently amended) The method of claim 20, wherein the step of detecting activity of the reporter molecule ~~activity is achieved by~~ comprises cytometric analysis of a ~~fluoreseent~~ fluoresence or light ~~emitting reporter molecule~~ emission.

23. (Canceled)

24. (Currently amended) The method of claim ~~[[23]]~~20, wherein the step of isolation of reporter-active ~~isolating antibody secreting cells~~ [[is by]] within the population of genetically modified cells based on activity of the reporter molecule comprises flow cytometry, laser scanning cytometry, or chromatography and/or other equivalent procedure.

25. (Currently amended) The method of claim ~~[[23]]~~20, further comprising a step of selecting reporter-active cells using based on expression of further selection markers.

26-47. (Canceled)

48. (Previously presented) The organism of claim 1, provided in the form of embryos.

49. (Previously presented) The organism of claim 1, wherein the reporter molecule is a fluorescent or light emitting reporter molecule.

50. (Currently amended) ~~[[A]]~~ An isolated genetically modified cell, wherein the genetic modification comprises the insertion of a reporter molecule-encoding sequence into an allele of the endogenous *Blimp (PRDM-1)* gene thereby creating a modified *Blimp* allele, and ~~wherein~~

expression of a polypeptide comprising the reporter molecule from the modified *Blimp* allele is under the control of endogenous *Blimp* regulatory elements, and wherein said genetically modified cell is capable of producing functional Blimp protein.

51. (Previously presented) The cell of claim 50, wherein said cell is in the form of gametes or embryonic stem cells.

52. (Previously presented) The cell of claim 50, wherein the modified *Blimp* allele encodes an mRNA transcript comprising a Blimp coding sequence and a reporter molecule coding sequence.

53. (Previously presented) The cell of claim 50, wherein the reporter molecule coding sequence is inserted within an intron of a *Blimp* allele.

54. (Previously presented) The cell of claim 50, wherein the modified *Blimp* allele is present in homozygous form.

55. (Previously presented) The cell of claim 50, wherein the modified *Blimp* allele is present in heterozygous form.

56. (New) The method of claim 20, wherein said population of genetically modified cells is derived from a cancerous or non-cancerous embryonic cell.

57. (New) The method of claim 20, wherein said population of genetically modified cells is obtained from a genetically modified non-human organism comprising said genetic modification.

58. (New) The method of claim 57, wherein said population of genetically modified cells is obtained from a lymphoid tissue of said genetically modified non-human organism.

59. (New) The method of claim 58, wherein said lymphoid tissue is selected from the group consisting of the bone marrow, spleen and lymph node.

60. (New) The method of claim 57, wherein said non-human organism is a laboratory test organism selected from the group consisting of a rodent, guinea pig, pig, duck, rabbit and sheep.

61. (New) A method for *in vitro* screening for agonists or antagonists of differentiation to antibody secreting cells, comprising:

- i) providing a population of genetically modified cells, wherein the genetic modification comprises the insertion of a reporter molecule-encoding sequence into an allele of the endogenous *Blimp* gene thereby creating a modified *Blimp* allele, and expression of a polypeptide comprising the reporter molecule from the modified *Blimp* allele is under the control of endogenous *Blimp* regulatory elements, and wherein said genetically modified cells are capable of producing functional Blimp protein and differentiating into antibody secreting cells;
- ii) contacting the population of genetically modified cells with an agent *in vitro*; and
- iii) detecting activity of the reporter molecule in the cell population,

wherein a change in the activity of the reporter molecule in the presence of said agent relative to in the absence of the agent indicates the ability of the agent to act as an agonist or antagonist of differentiation into antibody secreting cells.

62. (New) The method of claim 61, wherein said population of genetically modified cells is derived from a cancerous or non-cancerous embryonic cell.

63. (New) The method of claim 61, wherein said population of genetically modified cells is obtained from a genetically modified non-human organism comprising said genetic modification.

64. (New) The method of claim 63, wherein said population of genetically modified cells is obtained from a lymphoid tissue of said genetically modified non-human organism.

65. (New) The method of claim 64, wherein said lymphoid tissue is selected from the group consisting of the bone marrow, spleen and lymph node.

66. (New) The method of claim 63, wherein said non-human organism is a laboratory test organism selected from the group consisting of a rodent, guinea pig, pig, duck, rabbit and sheep.

67. (New) A method for *in vivo* screening for agonists or antagonists of differentiation to antibody secreting cells, comprising:

- i) providing a genetically modified non-human organism, wherein the genetic modification comprises the insertion of a reporter molecule-encoding sequence into an allele of the endogenous *Blimp* gene thereby creating a modified *Blimp* allele, and expression of a polypeptide comprising the reporter molecule from the modified *Blimp* allele is under the control of endogenous *Blimp* regulatory elements, and wherein said genetically modified non-human organism is capable of producing functional Blimp protein;
- ii) exposing said organism to an agent *in vivo*; and
- iii) detecting activity of the reporter molecule in said organism,

wherein a change in the activity of the reporter molecule in the presence of said agent relative to in the absence of the agent indicates the ability of the agent to act as an agonist or antagonist of differentiation into antibody secreting cells.

68. (New) The method of claim 67, wherein said non-human organism is a laboratory test organism selected from the group consisting of a rodent, guinea pig, pig, duck, rabbit and sheep.

69. (New) The method according to any one of claims 20, 61 or 67, wherein said modified *Blimp* allele encodes an mRNA transcript comprising a Blimp coding sequence and a reporter molecule coding sequence.

70. (New) The method of claim 69, wherein the reporter molecule coding sequence is inserted within an intron of a *Blimp* allele.

71. (New) The method of claim 69, wherein the modified *Blimp* allele is present in homozygous form.

72. (New) The method of claim 69, wherein the modified *Blimp* allele is present in heterozygous form.